April 2013

Arboviral Infection

Surveillance Protocol

Arboviruses endemic to the U.S. include Eastern equine encephalitis virus (EEE), La Crosse encephalitis virus (LAC), Saint Louis encephalitis virus (SLE), West Nile virus (WNV), Western equine encephalitis virus (WEE), and the tickborne Powassan encephalitis virus (POW). See other materials for information on non-endemic arboviruses (e.g., dengue fever and yellow fever)

Provider Responsibilities

1. Report suspect and confirmed cases of arbovirus infection (including copies of lab results) to the local health department within one week of diagnosis. Supply requested clinical information to the local health department to assist with case ascertainment.
2. Assure appropriate testing is completed for patients with suspected arboviral infection. The preferred diagnostic test is testing of virus-specific IgM antibodies in serum or cerebrospinal fluid (CSF). In West Virginia, appropriate arbovirus testing should include EEE, LAC, SLE, and WNV. Testing for a complete arboviral panel is available **free of charge** through the West Virginia Office of Laboratory Services (OLS).

Laboratory Responsibilities

1. Report positive laboratory results for arbovirus infection to the local health department within 1 week.
2. Submit positive arboviral samples to the Office of Laboratory Services within 1 week.
3. Appropriate testing for patients with suspected arboviral infection includes testing of virus-specific IgM antibodies in serum or CSF. In West Virginia, testing should routinely be conducted for WNV, EEE, SLE, and LAC. A complete arboviral panel is available free of charge through OLS. For more information go to: http://www.wvdhhr.org/labservices/labs/virology/arbovirus.cfm

Local Health Responsibilities

1. Conduct an appropriate case investigation.
    a. Contact the healthcare provider that ordered the laboratory test to obtain the clinical information on the WVEDSS form.
    b. If needed, contact the patient to obtain information regarding travel history.
    c. Conduct a home visit and perform an environmental assessment to identify potential risk factors for exposure to mosquitoes.
    d. Educate the patient and the patient's family on arbovirus prevention.
    e. Report all case data using WVEDSS.
2. Educate the public about arboviruses, especially regarding prevention measures. Late spring and early summer are optimal times to provide this education. A model

press release is available under "Tools for Local Health Departments" at: http://www.dhhr.wv.gov/oeps/disease/Zoonosis/Mosquito/Pages/Arbo.aspx

3. Educate providers and laboratories to report cases of arbovirus infection to the local health department in the patient's county of residence within one week of diagnosis.

State Health Responsibilities

1. Review completed case reports from local health departments within one week.
2. Report all confirmed and probable cases to CDC using ArboNET upon confirmation of case status.
3. Provide training and consultation to local health departments regarding case ascertainment and prevention for arbovirus infection.
4. Complete enhanced passive surveillance activities each spring. This includes release of a statewide HAN to healthcare providers, a laboratory letter, a training seminar, updates to arboviral information sheets, and release of a memo to local health departments.
5. Conduct yearly mosquito surveillance activities (see mosquito surveillance protocol)
6. Provide regular data feedback to local health departments and public health partners during arbovirus season (May-October).
7. Assure resources and equipment are available for laboratory testing and mosquito surveillance.
8. Encourage surveillance of dead birds and horses and provide necessary information and resources to conduct this surveillance.
9. Coordinate with other agencies, as needed, to monitor arboviral activity and respond to urgent situations.

Disease Prevention Objectives

1. Reduce disease risk through:
    a. Public education regarding use of personal protective measures
    b. Appropriate mosquito surveillance and control
2. Use mosquito surveillance data to provide timely notification to the public and local health departments of arboviral activity in mosquitoes.

Disease Control Objectives

1. Perform or increase mosquito control activities when human arboviral cases or increased arboviral mosquito activity is detected in an area.
2. Provide or increase public education when human arboviral cases or increased arboviral mosquito activity is detected in an area.

Disease Surveillance Objectives

1. To identify and monitor the epidemiologic characteristics of human arbovirus infections in West Virginia.
2. To identify the geographic distribution of non-human cases of arboviral infection through testing of dead birds and suspected equine arbovirus cases.
3. To identify and characterize (by species and geographic distribution) arboviral-infected mosquitoes and evaluate their potential to transmit novel or travel-associated arboviruses such as dengue and chikungunya.
4. To identify new or invasive mosquito species not previously identified in West Virginia that could be capable of transmitting arboviruses.
5. To provide early notification of increased arboviral mosquito activity through trapping and testing of mosquitoes.

Public Health Significance

After its introduction in 1999, West Nile virus expanded its territory across the United States. West Nile called attention to the weakened public health infrastructure for arbovirus surveillance in the United States. Due to this concern, federal money was allocated to improve public health infrastructure, including laboratory diagnostic and medical entomology capacity. Travel-associated outbreaks of chikungunya and dengue virus have further called attention to the possibility of introduction of new arboviruses into the United States.

The occurrence of arboviral disease outbreaks is unpredictable; thus public health officials should remain vigilant for increased activity during the summer months, which coincides with increased vector activity. SLE and EEE can occur in sometimes dramatic outbreaks at lengthy intervals with little or no apparent transmission in intervening years. Here are the types of surveillance that should be performed and the purpose of each type of surveillance:

1. **Dead Bird Surveillance**: The purpose of dead bird surveillance is to monitor the presence of WNV, EEE or SLE within the jurisdiction under surveillance.
2. **Mosquito Surveillance**: Mosquito surveillance is conducted to identify mosquito breeding sites and prioritize sites for abatement, and determine if disease-carrying adult mosquitoes are present. See mosquito surveillance plan.
3. **Equine Surveillance**: Horses may serve as an important indicator of WNV and EEE activity in the jurisdiction.
4. **Human Surveillance**: The purpose of human surveillance is to detect human arbovirus infection within the jurisdiction.

Regardless of the type of surveillance performed, the information collected should be used to prevent further human cases of disease. The ecology and public health aspects

of arboviruses are complex. West Virginia public health officials are encouraged to take the necessary time to educate themselves about these diseases.

In West Virginia, the major arbovirus of concern is LAC; however the largest number (10) of WNV human cases was reported during 2012. Birds positive for EEE were identified in 2002 in West Virginia. Twelve human cases of SLE were reported from West Virginia between 1964 and 2008, with the majority of cases occurring in 1975 during a national SLE epidemic. No human cases of Powassan have been identified in West Virginia; however, the virus was isolated from the brain of a sick fox in West Virginia in 1977 and the primary tick vector, *Ixodes cookei* has been documented in several West Virginia counties.

Clinical Description

Arboviral diseases are clinically indistinguishable from one another. They vary in terms of severity, long-term sequelae and the age groups most heavily affected. The most common manifestation is asymptomatic infection for WNV, LAC and SLE; while EEE is noteworthy for its low case-infection ratio and its high case-fatality rate. Other common clinical syndromes include 1) undifferentiated febrile illness, also referred to as 'febrile headache;' and 2) CNS infection, including aseptic meningitis, encephalitis or myelitis. Clinical presentations with nervous system involvement can be particularly variable and may involve the brain, spinal cord or nerves. The patient may present with syndromes mimicking a stroke or Parkinsonism, as well as tremors, movement disorders, neuritis, acute flaccid paralysis and/or SIADH.

Important definitions:

Acute flaccid paralysis: sudden onset of muscle weakness with hyporeflexia (decreased muscle reflexes) due to peripheral nerve or spinal cord involvement.

Aseptic meningitis: Symptoms of meningitis include fever, headache, photophobia, stiff neck and vomiting. Persons with aseptic meningitis have greater than 5 white blood cells in the spinal fluid and negative bacterial cultures. Meningitis means _inflammation of the meninges.' Meninges are the membranous lining around the brain. _Aseptic' means that there are no bacteria found (in the spinal fluid).

Encephalitis: literally means _inflammation of the brain.' These persons have fever and signs of central nervous system involvement, including: seizures, altered mental status, muscle weakness, sensory loss, or even movement disorders. On CT or MRI, focal or generalized swelling of the brain may be identified.

Febrile headache: is a self-limited illness characterized by fever and headache. Other signs and symptoms associated with this syndrome may include: rash, arthritis, weakness, vomiting and lymphadenopathy.

Myelitis: literally inflammation of the spinal cord. The spinal cord contains nerve fibers that support motor and sensory function. Myelitis results in weakness or paralysis, sensory changes and impaired bowel or bladder function.
Neuritis: literally inflammation of a nerve. Peripheral nerves are those outside of the brain or spinal cord. Neuritis prevents the nerve from functioning normally, so the person with neuritis may lose sensory (feeling, seeing, etc.) or motor (moving) function.
Parkinson's Disease: is a neurological disorder characterized by tremor, difficulty walking, movement and coordination. Parkinsonism refers to any condition that causes a movement disorder similar to Parkinson's Disease.
SIADH: Syndrome of inappropriate antidiuretic hormone results in hyponatremia (low blood sodium) due to excessive secretion of antidiuretic hormone.
While there is no way to clinically distinguish one arboviral infection from another, the arboviruses result in illness of varying clinical severity by age group and several occur in distinct regions of the country (Table 1).

Table 1. Clinical spectrum, high risk groups and geographic distribution of endemic North American arboviruses.

Virus	Case-Fatality Rate	Prevalence of Neurological sequelae	Age Groups Most Affected	Geographic Distribution in United States
Eastern equine encephalitis	36–70% of symptomatic cases	35% of surviving symptomatic cases	Children and the elderly	Atlantic and Gulf coastal areas, Great Lakes
La Crosse encephalitis	< 1% of all infections; ≈ 1% of hospitalized cases	3–12% of hospitalized cases	Children (primarily 15 years or younger)	Upper Midwestern, mid-Atlantic and southeastern states
St. Louis encephalitis	< 1% of all infections; 3–30% among symptomatic cases (higher in the elderly)	Unknown	Infants and elderly	Reported throughout U.S.; outbreaks in Mississippi Valley and Gulf Coast
West Nile encephalitis	< 1% of all infections; 12–14% among hospitalized cases (higher in the elderly)	Up to 50% of hospitalized patients at one year follow up	Elderly	Widespread; current incidence is greatest in Western U.S.
Western equine encephalitis	3–7% among symptomatic cases	15–30% (primarily among children <1 year)	Young children and the elderly	West of Mississippi River
Powassan	10–15% among symptomatic cases	Up to 50% of surviving symptomatic cases	Adults	New England, North Central states

Etiologic Agent

The viruses responsible for the endemic North American arboviruses belong to three distinct families: Togaviridae, Bunyaviridae, and Flaviviridae (Table 2).

Table 2. Family and genera of endemic North American arboviruses.

Virus	Etiologic Agent
Eastern equine encephalitis	family Togaviridae, genus *Alphavirus*
La Crosse encephalitis (California serogroup)	family Bunyaviridae, genus *Bunyavirus*
Saint Louis encephalitis	family Flaviviridae, genus *Flavivirus*
West Nile virus	family Flaviviridae, genus *Flavivirus*
Western equine encephalitis	family Togaviridae, genus *Alphavirus*
Powassan encephalitis	family Flaviviridae, genus *Flavivirus*

Reservoir

Reservoir species develop sufficiently high viremia such that a mosquito or tick can pick up virus from a blood meal and subsequently transmit the virus to other hosts. Horses and humans develop only low-level viremia and are referred to as dead-end hosts, meaning they are not important in transmission to other species.

The natural reservoirs for the endemic North American arboviruses vary depending on the specific virus and its transmission cycle but generally include birds or small rodents (Table 3).

Table 3. Endemic North American arboviruses and their reservoirs.

Virus	Reservoir
Eastern equine encephalitis	Wild birds (e.g., songbirds)
La Crosse encephalitis	Small wild rodents (e.g., chipmunks and squirrels)
Saint Louis encephalitis	Wild birds (e.g., house sparrow, pigeon, blue jay, and robin)
West Nile virus	Wild birds (e.g., crows, blue jays)
Western equine encephalitis	Wild birds (e.g., house finches and sparrows)
Powassan encephalitis	Small rodents, small wild carnivores (e.g., opossums, rabbits, groundhogs, squirrels, skunks, and foxes)

Mode of Transmission

Arboviruses are primarily spread through vectorborne transmission from the bite of an infected mosquito or infected tick (for POW only). See Table 4 for the primary vectors involved in human transmission. Five additional routes of infection for West Nile include transplantation, transfusion, breastfeeding, transplacental and occupational (laboratory workers). These modes of transmission represent a very small proportion of cases.

There is no documented evidence of direct person-to-person or animal-to-person transmission of arboviruses. There is a theoretical concern that a person may get WNV from handling live or dead infected birds, so people should avoid bare-handed contact

when handling dead animals, and use gloves or double plastic bags to place carcasses in garbage cans. People should ALWAYS wash hands after handing a sick or dead animal.

Table 4. Primary vectors for the endemic North American arboviruses.

Virus	Primary Arthropod Vector	Primary Species Important for Transmission to Humans, Horses
Eastern equine encephalitis	Mosquito	*Culex* species (*Cx. pipiens* and *Cx. quinquefasciatus* in the east, *Cx. nigripalpus* in Florida, and *Cx. tarsalis* and members of the *Cx pipiens* complex in western states); C*oquillettidia perturbans; Culiseta melanura*
La Crosse encephalitis	Mosquito	*Aedes triseriatus*, *Ae. Japonicas, Ae. albopictus*
Saint Louis encephalitis	Mosquito	*Culex* species (*Cx. pipiens* and *Cx. quinquefasciatus* in the east, *Cx. nigripalpus* in Florida, and *Cx. tarsalis* and members of the *Cx. pipiens* complex in western states)
West Nile virus	Mosquito	*Culex* species
Western equine encephalitis	Mosquito	*Culex tarsalis*
Powassan encephalitis	Tick	*Ixodes cookie, Ix. scapularis*

Incubation Period

The incubation periods for the endemic North American arboviruses are similar and range from 2 to 18 days, depending on the specific virus. Table 5 outlines the incubation period for each virus.

Table 5. Incubation period ranges for the endemic North American arboviruses.

Virus	Incubation Period (days)
Eastern equine encephalitis	3–10
La Crosse encephalitis (California serogroup)	5–15
St. Louis encephalitis	4–14
West Nile encephalitis	5–15
Western equine encephalitis	2–10
Powassan encephalitis	4–18

Period of Communicability

There is no direct person-to-person transmission of these viruses. See section on Modes of Transmission above.

Arboviral Infection

Surveillance Protocol

West Virginia Bureau for Public Health
Your Health Your Safety Our Purpose
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Outbreak Recognition

Because of low baseline incidence, any human (or equine) case of SLE, EEE, WEE or POW is defined as an outbreak. La Crosse is endemic in parts of West Virginia, so an outbreak of LAC is defined as cases over and above the expected or encroachment into an area of the state not previously known to have cases. The number of WNV cases varies each year but has been detected in multiple areas of the state. An outbreak of WNV is defined as cases over and above the expected number. DIDE should be notified immediately about outbreaks.

Case Definition

The 2011 case definition is the most current version (CSTE Position Statement Numbers: 10-ID-18, 10-ID-20, 10-ID-21, 10-ID-22, 10-ID-23, 10-ID-24).

Subtypes

California Serogroup Viruses, (i.e., California encephalitis, Jamestown Canyon, Keystone, La Crosse, Snowshoe hare, and Trivittatus viruses)
Eastern Equine Encephalitis Virus
Powassan Virus
St. Louis Encephalitis Virus
West Nile Virus
Western Equine Encephalitis Virus

Background

Arthropod-borne viruses (arboviruses) are transmitted to humans primarily through the bites of infected mosquitoes, ticks, sand flies, or midges. Other modes of transmission for some arboviruses include blood transfusion, organ transplantation, perinatal transmission, consumption of unpasteurized dairy products, breast feeding, and laboratory exposures.
More than 130 arboviruses are known to cause human disease. Most arboviruses of public health importance belong to one of three virus genera: *Flavivirus, Alphavirus, and Bunyavirus*.

Clinical Description

Most arboviral infections are asymptomatic. Clinical disease ranges from mild febrile illness to severe encephalitis. For the purposes of surveillance and reporting, based on their clinical presentation, arboviral disease cases are often categorized into two primary groups: neuroinvasive disease and non-neuroinvasive disease.

Neuroinvasive disease

Many arboviruses cause neuroinvasive disease such as aseptic meningitis, encephalitis, or acute flaccid paralysis (AFP). These illnesses are usually characterized by the acute onset of fever with stiff neck, altered mental status, seizures, limb weakness, cerebrospinal fluid (CSF) pleocytosis, or abnormal neuroimaging. AFP may result from anterior ("polio") myelitis, peripheral neuritis, or post-infectious peripheral demyelinating neuropathy (i.e., Guillain-Barré syndrome). Less common neurological manifestations, such as cranial nerve palsies, also occur.

Non-neuroinvasive disease
Most arboviruses are capable of causing an acute systemic febrile illness (e.g., West Nile fever) that may include headache, myalgias, arthralgias, rash, or gastrointestinal symptoms. Rarely, myocarditis, pancreatitis, hepatitis, or ocular manifestations such as chorioretinitis and iridocyclitis can occur.

Clinical criteria for diagnosis

A clinically compatible case of arboviral disease is defined as follows:
Neuroinvasive disease

- Fever (≥100.4°F or 38°C) as reported by the patient or a health-care provider, AND
- Meningitis, encephalitis, acute flaccid paralysis, or other acute signs of central or peripheral neurologic dysfunction, as documented by a physician, AND
- Absence of a more likely clinical explanation.

Non-neuroinvasive disease

- Fever (≥100.4°F or 38°C) as reported by the patient or a health-care provider, AND
- Absence of neuroinvasive disease, AND
- Absence of a more likely clinical explanation.

Laboratory Criteria for Diagnosis

- Isolation of virus from, or demonstration of specific viral antigen or nucleic acid in, tissue, blood, CSF, or other body fluid, OR
- Four-fold or greater change in virus-specific quantitative antibody titers in paired sera, OR
- Virus-specific IgM antibodies in serum with confirmatory virus-specific neutralizing antibodies in the same or a later specimen, OR
- Virus-specific IgM antibodies in CSF and a negative result for other IgM antibodies in CSF for arboviruses endemic to the region where exposure occurred, OR
- Virus-specific IgM antibodies in CSF or serum.

Case Classification

Confirmed

Neuroinvasive disease

A case that meets the above clinical criteria for neuroinvasive disease and one or more the following laboratory criteria for a confirmed case:

- Isolation of virus from, or demonstration of specific viral antigen or nucleic acid in, tissue, blood, CSF, or other body fluid, OR
- Four-fold or greater change in virus-specific quantitative antibody titers in paired sera, OR
- Virus-specific IgM antibodies in serum with confirmatory virus-specific neutralizing antibodies in the same or a later specimen, OR
- Virus-specific IgM antibodies in CSF and a negative result for other IgM antibodies in CSF for arboviruses endemic to the region where exposure occurred.

Non-neuroinvasive disease

A case that meets the above clinical criteria for non-neuroinvasive disease and one or more of the following laboratory criteria for a confirmed case:

- Isolation of virus from, or demonstration of specific viral antigen or nucleic acid in, tissue, blood, CSF, or other body fluid, OR
- Four-fold or greater change in virus-specific quantitative antibody titers in paired sera, OR
- Virus-specific IgM antibodies in serum with confirmatory virus-specific neutralizing antibodies in the same or a later specimen, OR
- Virus-specific IgM antibodies in CSF and a negative result for other IgM antibodies in CSF for arboviruses endemic to the region where exposure occurred.

Probable

Neuroinvasive disease

A case that meets the above clinical criteria for neuroinvasive disease and the following laboratory criteria:

- Virus-specific IgM antibodies in CSF or serum but with no other testing.

Non-neuroinvasive disease

A case that meets the above clinical criteria for non-neuroinvasive disease and the laboratory criteria for a probable case:

- Virus-specific IgM antibodies in CSF or serum but with no other testing.

Comment

Interpreting arboviral laboratory results

- **Serologic cross-reactivity.** In some instances, arboviruses from the same genus produce cross-reactive antibodies. In geographic areas where two or more closely-related arboviruses occur, serologic testing for more than one virus may be needed and results compared to determine the specific causative virus. For example, such

testing might be needed to distinguish antibodies resulting from infections within genera, e.g., flaviviruses such as West Nile, St. Louis encephalitis, Powassan, Dengue, or Japanese encephalitis viruses.

- **Rise and fall of IgM antibodies.** For most arboviral infections, IgM antibodies are generally first detectable at 3 to 8 days after onset of illness and persist for 30 to 90 days, but longer persistence has been documented (e.g, up to 500 days for West Nile virus). Serum collected within 8 days of illness onset may not have detectable IgM and testing should be repeated on a convalescent-phase sample to rule out arboviral infection in those with a compatible clinical syndrome.
- **Persistence of IgM antibodies**. Arboviral IgM antibodies may be detected in some patients months or years after their acute infection. Therefore, the presence of these virus-specific IgM antibodies may signify a past infection and be unrelated to the current acute illness. Finding virus-specific IgM antibodies in CSF or a fourfold or greater change in virus-specific antibody titers between acute- and convalescent-phase serum specimens provides additional laboratory evidence that the arbovirus was the likely cause of the patient's recent illness. Clinical and epidemiologic history also should be carefully considered.
- **Persistence of IgG and neutralizing antibodies.** Arboviral IgG and neutralizing antibodies can persist for many years following a symptomatic or asymptomatic infection. Therefore, the presence of these antibodies alone is only evidence of previous infection and clinically compatible cases with the presence of IgG, but not IgM, should be evaluated for other etiologic agents.
- **Arboviral serologic assays.** Assays for the detection of IgM and IgG antibodies commonly include enzyme-linked immunosorbent assay (ELISA), microsphere immunoassay (MIA), or immunofluorescence assay (IFA). These assays provide a presumptive diagnosis and should have confirmatory testing performed. Confirmatory testing involves the detection of arboviral-specific neutralizing antibodies utilizing assays such as plaque reduction neutralization test.
- **Other information to consider.** Vaccination history, detailed travel history, date of onset of symptoms, and knowledge of potentially cross-reactive arboviruses known to circulate in the geographic area should be considered when interpreting results.

Imported arboviral diseases Human disease cases due to Dengue or Yellow fever viruses are nationally notifiable to CDC using specific case definitions. However, many other exotic arboviruses (e.g., Chikungunya, Japanese encephalitis, Tick-borne encephalitis, Venezuelan equine encephalitis, and Rift Valley fever viruses) are important public health risks for the United States as competent vectors exist that could allow for sustained transmission upon establishment of imported arboviral pathogens. Health-care providers and public health officials should maintain a high index of clinical suspicion for cases of potentially exotic or unusual arboviral etiology, particularly in

international travelers. If a suspected case occurs, it should be reported to the appropriate local/state health agencies and CDC.

Preventive Interventions

There is currently no vaccine against human arboviruses.

Repellants such as DEET, oil of lemon eucalyptus, IR3535 and picaridin have demonstrated efficacy against mosquitoes.

Share these prevention messages with the public:

1. Empty standing water in old tires, cemetery urns, buckets, plastic covers, toys, or any other container where mosquitoes may breed.
2. Empty and change the water in bird baths, fountains, wading pools, rain barrels, and potted plant trays at least once a week if not more often.
3. Drain or fill temporary pools with dirt.
4. Keep swimming pools treated and circulating.
5. Keep rain gutters unclogged.
6. Use mosquito repellents according to the label directions. Apply sparingly to children before they play out of doors, and rinse children off with soap and water when they come back in. Do not apply repellent to the face and hands of young children because they may rub it in their eyes. Follow label directions and precautions closely.
7. Use head nets, long sleeves, and long pants if you venture into areas with high mosquito populations.
8. Make sure window and door screens are bug tight.

Treatment

Supportive; no specific treatment exists for arboviral infections.

Surveillance Indicators

1. Number of dead birds submitted for testing for arboviruses.
    a. Percentage of dead birds testing positive for arboviral infection
2. Number of mosquito pools collected and tested for arboviruses
    a. Evidence of increasing arboviral infection rates among tested mosquito pools during the season
3. Number of equine specimens submitted for testing for arboviruses.
    a. Percentage of equine specimens testing positive for arboviral infection
4. Percentage of human arboviral infection case specimens forwarded by OLS to CDC for laboratory confirmation (e.g., PRNT).

5. Proportion of cases with complete clinical investigation: Patient demographics, risk factor information (travel history, outdoor activities), and clinical symptoms.

6. Proportion of cases with a home visit completed for environmental evaluation, including GIS coordinates of location and patient and family education.

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